Remarks

Claims 1-45 are pending in the subject application. Applicants acknowledge that claims 4-9, 13-18, and 36-45 have been withdrawn from further consideration as being drawn to a non-elected invention. By this Amendment, claims 1, 2, and 10-12, have been amended, claims 3-9, 13-18, and 36-45 have been canceled, and claim 46 has been added. Support for the amendments and new claim can be found throughout the subject specification and in the claims as originally filed. Entry and consideration of the amendments and new claim presented herein is respectfully requested. Accordingly, claims 1, 2, 10-12, 19-35, and 46 are currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

As an initial matter, Applicants gratefully acknowledge the Examiner's indication that claims 2, 10, 11, 19-24, 32 and 34 are allowed.

The specification is objected to because of informalities. Applicants gratefully acknowledge the Examiner's careful review of the specification. In accordance with the Examiner's suggestion, Applicants have amended page 56, line 1, of the specification to place a filled circle between the parenthesis. Accordingly, reconsideration and withdrawal of the objection is respectfully requested.

The Action objects to the listing of references in the specification as not a proper information disclosure statement. Applicants submitted an Information Disclosure Statements in the subject application on January 21, 2004 and April 26, 2004 and note that all references listed in a specification need not be disclosed in an IDS.

Claims 1, 3, 12, 25-31, 33, and 35 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully assert that there is adequate written description in the subject specification to convey to the ordinarily skilled artisan that they had possession of the claimed invention. The Office Action rejects the claims on the basis that the recited polypeptide fragments embrace a substantial variety of peptide fragments obtained from SEQ ID NO: 8 (comprising at least 10 to 15 consecutive amino acids of SEQ ID NO: 8). Applicants respectfully submit that this issue is now moot with respect to claim 1 in view of the amendments made to the claim. The Office Action is argues that the as-filed specification fails to teach a

representative number of polypeptide fragments of SEQ ID NO: 8, defined by amino acid sequence or of a recitation of structural features common to the genus. The Office Action further supports its position with reference to *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997) and *Fiers v. Revel*, 984 F.2d 1167 (Fed. Cir. 1993). With respect to claims 3, 12 and 46, Applicants respectfully submit that the as-filed application and the present claims meet the written description requirements of 35 U.S.C. § 112, first paragraph.

Applicants respectfully submit that the Patent Office's reliance on *Fiers* and *Eli Lilly* in support of its position that the invention fails the written description requirement with respect to the recited fragments of SEQ ID NO: 8 is misplaced. In cases such as *Fiers* and *Eli Lilly*, the patent specifications at issue did not identify the sequence (structure) of any embodiment of DNA claimed therein (emphasis added). *See Eli Lilly*, 119 F.3d at 1567-68 (affirming a judgment that the claim requiring cDNA encoding human insulin was invalid for failing to provide an adequate written description where the specification described the human insulin A and B chain amino acid sequences encoded by the cDNA, but did not provide the nucleotide sequence for the cDNA itself); *Fiers*, 984 F.2d at 1167-68, 1170-71 (finding the written description insufficient where the patent claimed purified DNA encoding human fibroblast interferon-beta polypeptide, but the specification only disclosed a bare reference to DNA and suggested a process to sequence it).

In contrast, the instant specification teaches both the DNA and amino acid sequences of the claimed polypeptide. Further, the claims recite a "biologically active fragment" of SEQ ID NO: 8, wherein the fragments span that portion of SEQ ID NO: 8 having one of the biological activities disclosed within the specification at pages 22-23. Further, the phrase "biologically active" relates to a polypeptide that exhibits at least one of the LSR receptor activities (*e.g.*, a fatty acid binding site, a clathrin binding site, a transport signal, a leptin binding site, a RSRS motif, and/or a lipoprotein binding site). Indeed, the claims recite polypeptide fragments of SEQ ID NO: 8 defined by both amino acid sequence and a recitation of structural features common to the genus of fragments (embraced by the amino acids spans recited within the claims and as disclosed in Table 4 at page 21). The specification also discloses test data that indicates that the rat α polypeptide is capable of binding lipoproteins in the absence of other elements of the receptor (see page 68, line 30 through page 70, line 15 and Figures 15-16). Thus, polypeptides containing the recited spans of amino acids

would reasonably be expected to have the biological activities associated with the structural regions (even in the absence of the other elements of the receptor, such as the β subunit). Accordingly it is respectfully submitted that the as-filed specification and instant claims meet the written description requirement under both the *Eli Lilly* and *Piers* analysis. Accordingly reconsideration and withdrawal of the rejection is respectfully requested.

With respect to newly presented claim 1, Applicants respectfully submit that this claim also complies with the written description requirement. As is noted in the specification, the murine and rat form of the LSR α polypeptide exhibit 80.2 and 82.2 percent identity to the human α polypeptide (see page 19, lines 15-22) and all three polypeptides exhibit the functional domains disclosed within the as-filed specification. In view of this disclosure, it is respectfully submitted that the as-filed specification provides adequate written description for polypeptides having at least 90% homology to the polypeptide of SEQ ID NO: 8 and teaches various amino acids tolerant of substitution such that the biological activity of the claimed polypeptide is not abolished (see, for example, Figure 2).

Claims 1, 3, 12, 25-31, 33 and 35 are rejected under 35 U.S.C. § 112, first paragraph, as non-enabled by the subject specification. The Office Action argues the as-filed specification fails to enable one skilled in the art to make and use a polypeptide comprising fragments of SEQ ID NO: 8. The Office Action also argues that the claims recite a polypeptide that may comprise only one of the disclosed biologically active fragments and that the rest of the polypeptide may be completely different. It is also argued that certain positions in a polypeptide sequence are critical to the protein's structure/function relationship and that these regions can tolerate only relatively conservative substitutions or no substitutions. The Office Action further argues that the specification does not teach those amino acids that are tolerant to change and supports its arguments with references related to TGF-β and the effects of substituting non-essential amino acids within the polypeptide.

Applicants respectfully submit that the analysis undertaken by the Patent Office in this regard has failed to account for the teaching of three different α LSR subunits that exhibit about 80% sequence identity and that the references cited in support of the Office Action's position are not dispositive of this issue in view of this teaching by Applicants. Applicants submit that the sequence alignment provided in Figure 2 would clearly indicate to one skilled in the art those amino acids tolerant of substitution without complete abolition of biological function. Indeed, the FFA functional

domain exhibits some degree of tolerance to amino acid changes as evidenced by the alignment provided in Figure 2. Further, and as noted by the Office Action, the specification teaches methods of producing muteins and fusion proteins that can contain fragments of SEQ ID NO: 8 and methods of screening such polypeptides for the recited biological activity. Applicants also submit, with respect to those polypeptides that bind or internalize leptin or lipoproteins, that the as-filed specification teaches those portions of the polypeptides required for this function and that screening polypeptides having such domains does not involve undue experimentation. Applicants respectfully assert that that the claims are enabled by the subject specification. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Claim 1 is rejected under 35 U.S.C. § 102(b) as being anticipated by Steingrimsson *et al.*, Database UniProt_7.2, Accession No. Q61143 (1996). The Office Action indicates that the polypeptide of Steingrimsson *et al.* comprises an amino acid fragment that is 100% identical to several stretches of the polypeptide of SEQ ID NO: 8 and comprising more than 10 to 15 consecutive amino acids. In view of the amendment to claim 1, Applicants believe that this rejection is now moot. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b) is respectfully requested.

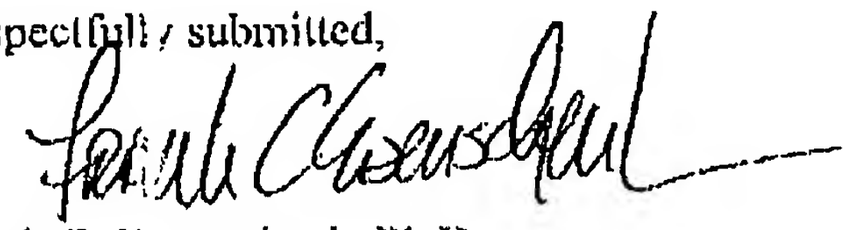
It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants' agreement with or acquiescence in the Examiner's position. Applicants expressly reserve the right to pursue the invention(s) disclosed in the subject application, including any subject matter canceled or not pursued during prosecution of the subject application, in a related application.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 9-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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